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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/674,090	03/01/2001	Yoav Eichen	RCP-PT009	1528

3624 7590 04/30/2009

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EXAMINER	
PANDE, SUCHIRA	

ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
04/30/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/674,090	EICHEN ET AL.	
	Examiner	Art Unit	
	SUCHIRA PANDE	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-9,18-20,22-28,35-39,41,43-45,47-51,53-57,60-63 and 65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4-9, 18-20, 22-28, 35-39, 41, 43-45, 47-51, 53-57, 60-63 and 65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

1. Amendment filed on February 17, 2009 is acknowledged. Applicant has amended claim 24; cancelled claims 2-3, 10-17, 21, 29-34, 40, 42, 46, 52, 58-59, 64, 66; currently claims 1, 4-9, 18-20, 22-28, 35-39, 41, 43-45, 47-51, 53-57, 60-63 and 65 are active and will be examined in this action.

Response to Arguments

Re 112 1st rejections of claims 55, 56, 60-63 and 65

2. Applicant's arguments, filed on February 17, 2009 with respect to claims 55, 56, 60-63 and 65 have been fully considered and are persuasive. The 112 1st written description and new matter rejections of claims 55, 56, 60-63 and 65 has been withdrawn.

Re 102 rejections of claims 1, 4-9, 18-20, 22-28, 45 and 57 over Mroczkowski et al.

3. Applicant's arguments filed February 17, 2009 have been fully considered but they are not persuasive. Each allegation or argument presented is being addressed below:

1) Applicant alleges Mroczkowski et al. do not teach a "recognition moiety positioned in the gap and bound to the substrate".

Applicant has defined target in the specification as "—an entity, which is to be assayed in a sample." While Recognition moiety is defined as "---an entity which specifically binds the target." Accordingly in the context of present invention any member of the antigen-antibody pair taught by Mroczkowski et al.

can be the target or recognition moiety respectively depending on which is the entity to be assayed. Hence Mroczkowski et al. does teach a "recognition moiety positioned in the gap and bound to the substrate".

2) On bottom of page 18 and page 19 Applicant is arguing limitations that refer to competitive assay. Applicant is reminded that competitive assay is not a limitation that is recited in instant claims. Hence arguments that refer to above non limitation are not being considered further.

3) Applicant alleges Mroczkowski does not disclose two components of step (c) of claim 1 namely:

(i) a solution comprising nucleation-center forming entities for binding to components of said target if said target is present in the sample;

and

(ii) a combination of metal ions and a reducing agent to allow formation of said conductive substance on said entities.

See page 15 lines 5-9 where solution containing antibody coated on gold particles is taught. Thus Mroczkowski et al. teach solution comprising nucleation-center forming entities. Also see page 18 lines 22-31 where they teach if gold particles are used as the particles to which one of the binding substances are bound, silver enhancement may be used to form a conductive silver coating over the aggregates. Further see page 25, lines 12-29 where Silver enhancement process is described in detail there fixative solution used contains ammonium thiosulfate, acetic acid, sodium metabisulfite, sodium tetraborate and aluminum sulfate. Thus teaching by teaching use of an enhancement reagent containing

silver lactate solution and a fixative solution taught above Mroczkowski et al. do teach (ii) a combination of metal ions and a reducing agent to allow formation of said conductive substance on said entities.

Thus contrary to Applicant's allegation Mroczkowski et al. does teach both components (i) and (ii) of claim 1 step (c).

Thus 102 rejections of claims 1, 4-9, 18-20, 22-23, 25-28 and 57 over Mroczkowski et al. are still valid and are being maintained.

Regarding claims 24 and 45, Applicant correctly points out Mroczkowski et al. do not teach the newly added limitation. Applicant has amended claim 24 to add limitations of claim 29 that has now been cancelled. Limitation of claim 29 was not taught by Mroczkowski et al. Hence Mroczkowski et al. do not teach currently amended claim 24. Accordingly rejection of claims 24 and its dependent claim 45 over Mroczkowski et al. is not valid and is being withdrawn.

Examiner will reject claim 24 and its dependent claim 45 over new art that teaches all the elements of the amended claim 24 and 45. Hollis et al. was used to teach limitation of former claim 29. Hence amended claim 24 and 45 will be rejected over Mroczkowski et al. in view of Hollis et al.

Re 103 rejections of claims 29, 43-44, 47-51, 55-56 and 65 over Mroczkowski et al. as applied to claims 1, 25, 26, 35 and 37 above further in view of and Hollis et al.

4. Since rejections of claims 1, 25, 26, 35 and 37 over Mroczkowski et al. are is being maintained. Accordingly rejections of claims 29, 43-44, 47-51, 55-56 and 65 further in view of Hollis et al. are also valid and are being maintained.

Re 103 rejections of claims 35, 37, 38 and 41 over Mroczkowski et al. as applied to claims 18 in view of Olsen

5. Since rejection of claim 18 over Mroczkowski et al. is being maintained. Accordingly rejections of claims 35, 37, 38 and 41 over Mroczkowski et al. further in view of Olsen is also valid and is being maintained.

6. As pointed out above rejection of claim 24 over Mroczkowski et al. is not valid any more. Hence rejection of claim 39 that depends from claim 24 over Mroczkowski et al. in view of Olsen is not valid and is being withdrawn.

Re 103 rejections of claims 36, 53-54 and 60-63 over Mroczkowski et al. and Olsen as applied to claims 35 and 37 further in view of Hollis et al.

7. Since rejection of claims 35 and 37 over Mroczkowski et al. and Olsen is being maintained. Accordingly rejections of claims 36, 53-54 and 60-63 further in view of Hollis et al. is being maintained.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Examiner is considering the claims directed to a system (claim 1); claims directed to a method for assaying (claims 25-26); together in claim 1 as both the system and method claimed contain common elements recited in claim 1. Furthermore they are directed to same invention namely assaying one or more

targets in a sample and all the claims share the limitations listed in claim 1. Additional limitations are addressed under the specific claims no.

1. Claims 1, 4-9, 18-20, 22-23, 25-28 and 57 are rejected under 35 U.S.C. 102(b) as being anticipated by Mroczkowski et al. (WO 90/05300; cited in the IDS).

Regarding claims 1 and 25-26 Mroczkowski et al. teach a system, a method, an assay device for assaying one or more targets in a sample comprising:

(a) an assay device having one or more assay sets (see page 18 lines 1-8 where multiple assay sets are taught), the assay sets comprising at least two electrodes, a substrate, and a recognition moiety; the electrodes positioned on the substrate and separated by a gap (Fig. 1, 2, 4, 6, 7, 8; page 6, lines 14-22; page 11, lines 5-35; page 12, lines 1-33; page 13, lines 6-27; page 14, lines 14-22; page 21; page 22, lines 1-27); the recognition moiety positioned in the gap and bound to the substrate (Fig. 1, 2, 4, 6, 7; page 5, lines 21-35; page 6, lines 23-33; page 9, lines 5-14; page 10, lines 7-23);,

the recognition moiety (see page 5 line 29 where antibodies= recognition moiety are taught) being capable of specific binding to a component of a target selected from the group consisting of a bacterium, a virus, and a cell (see page 5 line 6-10 where detection of antigens in the fluids or tissues of human or animals is taught. By teaching antigens Mroczkowski et al. teach a bacterium, a virus, and a cell which all have antigens on their surfaces);

(b) an electric or electronic module arranged and configured to measure electric conductance between the at least two electrodes of each assay set (see page 8 lines 8-14);

(c) reagents formulated to deposit a conductive substance onto a complex formed between said recognition moiety and said target, wherein the reagents comprise: (i) a solution comprising nucleation-center forming entities for binding to components of said target if said target is present in the sample (page 15, lines 9-19; page 20, lines 11-33; page23, lines 6-15; page 25, lines 2-11)

; and (ii) a combination of metal ions and a reducing agent to allow formation of said conductive substance on said entities, and wherein the conductive substance, when deposited onto the complex, forms a conductive bridge between the at least two electrodes of a set (page 18, lines 22-31; page 25, lines 12-29); and

(d) means for determining whether the one or more targets are in the sample as a result of the extent of electric conductance between the at least two electrodes of each assay set (page 3, lines 1-11; page 7, lines 31-38; page 8, lines 1-14; page 9, lines 27-38; page 10; page 11, lines 1-4; page 24, 25; page 26, lines 1-27).

Regarding claim 25, Mroczkowski et al. teach step a) reacting a sample which may or may not have targets with a first reagent solution to bind nucleation center-forming entities to said targets (see page 6 lines 1-13 where patient and control samples are taught, thus teaching reacting a sample which may or may

not have targets with a first reagent solution to bind nucleation center-forming entities to said targets).

Regarding claim 26, Mroczkowski et al. teach steps c) and d) namely

(c) contacting said device with a first reagent solution comprising monomers of a conductive polymer such that said monomers can bind to complexes formed between the targets and recognition moieties (see page 14 lines 23-33 where gold particles or gold coated polystyrene spheres are taught as monomers);

(d) treating said device such that said monomers will polymerize to form a conducting polymer, such that upon polymerization of the monomers a conductive bridge between the at least two electrodes of at least one set is formed (see page 14 line 23 where layers of suitable conducting material such as gold etc is taught, by teaching conducting layer of gold, Mroczkowski et al. inherently teach polymerization of monomers to form a conducting polymer, see page 33 claim 5 steps 4 and 5; where coating aggregates with electrically conductive substance and measuring a change in current flow through said circuit caused by the presence of said aggregates in said channel is taught. Thus by teaching the flow of current through circuit Mroczkowski et al. teach formation of a conductive bridge between the at least two electrodes of at least one set is formed).

Thus all the elements recited in claims 1, and 25-26 are anticipated by Mroczkowski et al.

Regarding claims 4, and 6, Mroczkowski et al. teach wherein said nucleation-center forming entities are colloid particles (claim 4) and colloid gold particles (claim 6) (see page 9 line 35 where colloidal gold is taught).

Regarding claims 5, and 7, Mroczkowski et al. teach wherein said nucleation-center forming entities are metal complexes, clusters, or complexes and clusters-claim 5 and metal complexes or clusters are gold complexes or gold clusters. (see page 14 lines 29-33 where plastic particles having a conductive metal coating, especially gold-coated polystyrene spheres are taught)

Regarding claims 8 and 9, Mroczkowski et al. teach platinum (see page 14 line 28)

Regarding claim 18, Mroczkowski et al. teach a system comprising a plurality of assay sets of electrodes (see fig. 8 page 17 lines 4-17).

Regarding claim 19, Mroczkowski et al. teach wherein all assay sets of electrodes are for assaying the same component of the same target (see page 29 example 4 and Table 4 where all assay sets were designed to detect rabbit IgG).

Regarding claim 20, Mroczkowski et al. teach wherein different assay sets of electrodes or different groups of assay sets are for assaying different targets (see page 5 lines 6-9 where different targets are taught). (see fig. 8 and 9 where multiplexing is taught and measurement of conductance from each assay set is performed using ohmmeter).

Regarding claims 22 and 23, Mroczkowski et al. teach when the target is a protein or polypeptide and the recognition moiety is a protein-binding molecule

which specifically binds to the target protein (see page 5 lines 21-35 where target antigen 12A is taught along with antibody 15A is taught as the recognition moiety which is a protein-binding molecule which specifically binds to the target protein 12A).

Regarding claim 27, Mroczkowski et al. teach comprising before step (a) reacting the sample with a second reagent solution containing entities which can form nucleation centers for growing therefrom a conductive polymer from said monomers, such that said entities bind to said targets if present in the sample (see page 9 lines 33—36 where preincubation is omitted and directly sample 11A and colloidal gold 13A is reacted. Here colloidal gold 13A a second reagent solution containing entities which can form nucleation centers for growing therefrom a conductive polymer from said monomers, such that said entities bind to said targets if present in the sample).

Regarding claim 28, Mroczkowski et al. teach comprising after step (a) contacting said assay device with a second reagent solution containing entities which can form nucleation centers for growing therefrom a conductive polymer from said monomers, such that said entities bind to said targets if bound to said recognition moieties (see page 10 line 14 where second, conductively labeled antibody is taught as a second reagent solution containing entities which can form nucleation centers for growing therefrom a conductive polymer from said monomers, such that said entities bind to said targets if bound to said recognition moieties) .

Regarding claim 57, Mroczkowski et al. teach further comprising a sample which may or may not have the target (see page 8 lines 31-33 where patient sample 11A is taught it may or may not contain antigen 12A in the sample 11A thus teaching a sample which may or may not have the target) .

Thus claims 1, 4-9, 18-20, 22-23, 25-28 and 57 are anticipated by Mroczkowski et al.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 24, 43-45, 47-51, 55-56 and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mroczkowski et al. (WO 90/05300;

cited in the IDS) as applied to claims 1, 25, 26, 35 and 37 above further in view of and Hollis et al. (U.S. Patent No. 5,653,939 A previously cited).

Regarding claim 24 Mroczkowski et al. teach a method for assaying the presence or absence of one or more biological targets in a sample comprising:

(a) providing an assay device having one or more assay sets (see page 18 lines 1-8 where multiple assay sets are taught), the assay sets comprising at least two electrodes, a substrate, and a recognition moiety; the electrodes positioned on the substrate and separated by a gap (Fig. 1, 2, 4, 6, 7, 8; page 6, lines 14-22; page 11, lines 5-35; page 12, lines 1-33; page 13, lines 6-27; page 14, lines 14-22; page 21; page 22, lines 1-27); the recognition moiety positioned in the gap and bound to the substrate (Fig. 1, 2, 4, 6, 7; page 5, lines 21-35; page 6, lines 23-33; page 9, lines 5-14; page 10, lines 7-23);,

the recognition moiety (see page 5 line 29 where antibodies= recognition moiety are taught) being capable of specific binding to a component of a target (see page 5 line 6-10 where detection of antigens in the fluids or tissues of human or animals is taught. By teaching antibody-antigen interaction Mroczkowski et al. teach the recognition moiety being capable of specific binding to a component of a target);

(b) contacting said assay device with a sample which may or may not have the target under conditions permitting binding of targets, if any, present in the sample to specific recognition moieties to form a complex (see Fig 1 where antigen 12A is contacted with antibody 15A as depicted in panel 1C and IE where formation of antigen/antibody complex is shown. In panel 2A no antigen is

mixed with antibody 15B. Thus Mroczkowski et al. teach contacting said assay device with a sample which may or may not have the target under conditions permitting binding of targets, if any, present in the sample to specific recognition moieties to form a complex---see panel 1E and 2E where complex formed is shown).

(c) contacting said assay device with reagents to deposit a conductive substance onto the complex formed between said recognition moiety and said target, such that the conductive substance deposits onto the complex and forms a conductive bridge between said at least two electrodes (see Fig. 1 where electrically conductive metallic particles 14 A are bound to base 22A due to the binding reaction between antigen 12A and antibody (15 A) to thereby form aggregates (35A) of electrically conductive particles (14A) between at least two electrodes 23A and 23B. Thus teaching contacting said assay device with reagents to deposit a conductive substance onto the complex formed between said recognition moiety and said target, such that the conductive substance deposits onto the complex and forms a conductive bridge between said at least two electrodes) ;

(d) connecting said at least two electrodes to an electric or electronic module to measure conductance between said at least two electrodes (see page 8 lines 8-14 where connection to ohmmeter to measure conductance between said at least two electrodes is taught); and

(e) determining conductance between said at least two electrodes, wherein conductance above a threshold conductance indicates the presence of a

respective target in the sample while conductance below a threshold conductance indicates the absence of any targets in the sample (page 8 lines 27-page 9 lines 1-4 where measurement of conductance of control vs. actual test samples is taught and resistance values corresponding to specific antigen levels in the sample are taught thus teaching conductance of threshold values the negative control provides the lower threshold and resistance values of specific antigen levels are all above this threshold conductance).

Regarding claim 24, Mroczkowski et al. do not teach wherein the respective targets are nucleic acid molecules and the respective recognition moieties are oligonucleotides, the respective recognition moiety has a sequence which is complementary to at least a portion of the respective target;

Regarding claim 24, Hollis et al. teaches wherein the respective targets are nucleic acid molecules and the respective recognition moieties are oligonucleotides, the respective recognition moiety has a sequence which is complementary to at least a portion of the respective target; (see col. 6 lines 35-52).

Regarding claim 43, Hollis et al. teach wherein said one or more targets are one or more nucleic acid sequences (see col. 6 lines 48-49).

Regarding claim 44, Hollis et al. teach wherein said recognition moiety is an oligonucleotide having a sequence complementary to at least a portion of sequence of one of said one or more targets (see col. 6 lines 42-52).

Regarding claim 45, Mroczkowski et al. teach further comprising contacting said assay device with a first reagent solution to form nucleation-

center forming entities for depositing onto or binding to complexes formed between a target and a recognition moiety (see page 15, lines 9-19; page 20, lines 11-33; page23, lines 6-15; page 25, lines 2-11).

Regarding claims 47, 48 Hollis et al. teach wherein said targets are nucleic acid molecules and the recognition moieties are oligonucleotides, each of which has a sequence which is complementary to a nucleic acid molecule of said target (see claims 43 and 44 above).

Regarding claims 49, 50, 51 Hollis et al. teach wherein said targets are selected from the group consisting of a bacterium component, a virus component, and a cell component (see col. 1 lines 20-26).

Regarding claim 55 Hollis et al. teach wherein said means comprises a computer (see col. 7 line 4 where computer is taught).

Regarding claim 56 Hollis et al. teach wherein said means comprises a scanner for analyzing a plurality of assay sets (see col. 12 lines 10-12 where scanner is taught).

Regarding claim 65, Mroczkowski et al. teach a system for assaying one or more targets in a sample comprising:

(a) an assay device having one or more assay sets (see page 18 lines 1-8 where multiple assay sets are taught),

the assay sets comprising at least two electrodes (see Fig. 1 and 2. Elements 23 and 24 shown in figs a 23A and 24A in Fig. 1 and 23B and 24B in Fig. 2 are at least two electrodes. Also see page 6 lines 20- 21)

and a recognition moiety immobilized to each of the electrodes (see page 10 lines 7-13 where immobilized antibody=recognition moiety is taught),

each recognition moiety being an antibody capable of specific binding to an epitope of a target selected from the group consisting of a bacterium, a virus, and a cell (see page 5 line 6-10 where detection of antigens in the fluids or tissues of human or animals is taught. By teaching antigens Mroczkowski et al. teach an epitope of a target selected from the group consisting of a bacterium, a virus, and a cell which all have antigenic epitopes on their surfaces);

(b) an electric or electronic module arranged and configured to measure electric conductance between the at least two electrodes of each assay set (see page 8 lines 8-14);

(c) reagents formulated to deposit a conductive substance onto a complex formed between said recognition moiety and said target, wherein the reagents comprise: (i) a solution comprising nucleation-center forming entities for binding to components of said target if said target is present in the sample (page 15, lines 9-19; page 20, lines 11-33; page23, lines 6-15; page 25, lines 2-11)

; and (ii) a combination of metal ions and a reducing agent to allow formation of said conductive substance on said entities, and wherein the conductive substance, when deposited onto the complex, forms a conductive bridge between the at least two electrodes of a set (page 18, lines 22-31; page 25, lines 12-29); and

Regarding step d) Mroczkowski et al. teach microelectronics for determining whether the one or more targets are in the sample as a result of the

extent of electric conductance between the at least two electrodes of each assay set (See page 3, lines 1-11; page 7, lines 31-38; page 8, lines 1-14; page 9, lines 27-38; page 10; page 11, lines 1-4; page 24, 25; page 26, lines 1-27).

Regarding step d) Mroczkowski et al. do not teach a computer as recited in the presently amended claim.

Regarding step d) Hollis et al. teach a computer that is used for collecting and processing data (see col. 8 lines 61-65 where detection by means of a monolithically integrated charge-coupled device (CCD) is taught to detect presence or absence of hybridized molecules. By teaching a monolithically integrated charge-coupled device (CCD) Hollis et al. teach a computer).

Hollis et al. also teach detection of an epitope of a target selected from the group consisting of a bacterium, a virus, and a cell (see col. 18 lines 47-52).

It would have been prime facie obvious to one of ordinary skill in the art to combine the computer taught by Hollis et al. in the microelectronic system taught by Mroczkowski et al. at the time the invention was made. The motivation to do so is provided by Hollis et al. who state “The present invention can be used in connection with detection of targets which are molecular structures other than DNA or RNA, such as cells and antibodies.-----The technology described here employs those well understood binding interactions in a new microelectronic detection scheme. The commercial application of the methodology is for use to detect the presence of any of hundreds of thousands of different antibodies or other proteins, simultaneously, in a blood sample or other biological fluid. This is particularly useful in blood typing, the detection of viral infection such as AIDS, or

the diagnosis of cancer." (see col. 18 lines 3-53). Thus one of ordinary skill can immediately see the advantages of using a computer to process the huge amount of data that will be generated using these micro fabricated device resulting in more accurate, cheaper, faster and more efficient processing of multiple clinical samples as compared to manually recording the conductivity measurements obtained from the microelectronic circuits taught by Mroczkowski et al.

13. Claims 35, 37, 38 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mroczkowski et al. (WO 90/05300; cited in the IDS) as applied to claim 18 in view of Olsen (US pat. 5,614,832 issued March 25, 1997 previously cited).

Regarding claims 35, Mroczkowski et al. teach an electronic device for determining the presence or absence of one or more targets in a sample comprising:

an integrated circuit (see Fig. 8) comprising a first group of N1 conductors (see fig. 7 element 51 is first group of N1 conductors)

and a second group of N2 conductors (see fig. 7 element 52 is second group of N2 conductors), defining between them NlxN2 junctions (fig,. 7 element 53), each such junction being formed with an electronic module comprising two electrodes (fig. 8 layer 23 and 24 are electrodes), each electrode linked to or defined as an integral portion of one of the conductors (element 61 and 62 in Fig. 8 are conductors) and supported by a common substrate (base 22 in Fig. 8 is common substrate),

whereby a current flowing between one conductor of the first group to one conductor of the second group of conductors defines a single junction point between them (see page 18 lines 9-21 where Fig. 9 is described); each pair of electrodes forming part of an assay set (see fig. 8 where 23/24 each pair is shown to form an assay set),

each assay set having a recognition moiety for binding to a component of a target (see page 5 line 29 where antibodies= recognition moiety are taught) selected from the group consisting of a bacterium, a virus, and a cell (see page 5 line 6-10 where detection of antigens in the fluids or tissues of human or animals is taught. By teaching antigens Mroczkowski et al. teach a bacterium, a virus, and a cell which all have antigens on their surfaces), the recognition moiety bound to the substrate and positioned between the electrodes (see page 18 lines 3-8 where each assay set composed of pair of layers 23 and 24 is taught to have a different recognition moiety or no recognition moiety—for negative control or same recognition moiety bound to the substrate and positioned between the electrodes is taught) ;

the assay sets adapted to accept reagents formulated to deposit a conductive substance onto a complex formed between said recognition moiety and said target, wherein said reagents comprise:

(i) a solution comprising nucleation-center forming entities for binding to components of said target if said target is present in the sample (page 15, lines 9-19; page 20, lines 11-33; page23, lines 6-15; page 25, lines 2-11)

; and (ii) a combination of metal ions and a reducing agent to allow formation of said conductive substance on said entities, (page 18, lines 22-31; page 25, lines 12-29); and

means for determining whether the one or more targets are in the sample as a result of the extent of electric conductance between the two electrodes of each assay set (see page 25 line 28-29 where ohmmeter is taught as a means for determining whether the one or more targets are in the sample as a result of the extent of electric conductance between the two electrodes of each assay set).

Regarding claim 37, Mroczkowski et al. teach an electric device for determining the presence or absence of one or more targets in a sample comprising:

a microelectronic device having a plurality of layers, with a first group of conductors being defined as stripes in one or more first layers and a second group of conductors being defined as stripes in one or more second layers of the device with each of said second layers being separated from a first layer by a non-conductive substance, electrodes of the device being formed as open ends of the conductors by openings or cut-outs in a vertical direction through the layers (see section D photolithography on page 21 lines 21-page 22 lines 1-27 where formation of microelectronic device with above features is described);

each pair of electrodes forming part of an assay set, each assay set having a recognition moiety for binding to a component of a target selected from the group consisting of a bacterium, a virus, and a cell (see page 5 line 6-10

where detection of antigens in the fluids or tissues of human or animals is taught. By teaching antigens Mroczkowski et al. teach a bacterium, a virus, and a cell which all have antigens on their surfaces) bound to one or more layer in the vertical opening or cut-out (this is the gap described in claim 1); wherein the assay sets are adapted to accept reagents formulated to deposit a conductive substance onto a complex formed between said recognition moiety and said target, wherein said reagents comprise:

(i) a solution comprising nucleation-center forming entities for binding to components of said target if said target is present in the sample (page 15, lines 9-19; page 20, lines 11-33; page23, lines 6-15; page 25, lines 2-11); and

(ii) a combination of metal ions and a reducing agent to allow formation of said conductive substance on said entities (page 18, lines 22-31; page 25, lines 12-29), and

means for determining whether the one or more targets are in the sample as a result of the extent of electric conductance between the pair of electrodes of each assay set (see page 25 line 28-29 where ohmmeter is taught as a means for determining whether the one or more targets are in the sample as a result of the extent of electric conductance between the two electrodes of each assay set).

Regarding claims 38, Mroczkowski et al. teach wherein the device is an electronic device for determining one or more targets in a sample, comprising:

an integrated circuit (see Fig. 8) comprising a first group of N1 conductors (see fig. 7 element 51 is first group of N1 conductors)

and a second group of N2 conductors (see fig. 7 element 52 is second group of N2 conductors), defining between them NlxN2 junctions (fig,. 7 element 53), each such junction being formed with an electronic module comprising two electrodes (fig. 8 layer 23 and 24 are electrodes), each electrode linked to or defined as an integral portion of one of the conductors (element 61 and 62 in Fig. 8 are conductors) and

each pair of electrodes forming part of an array set (see fig. 8 and 9 where array sets are shown), each array set having a recognition moiety bound to at least one of the electrodes (see page 24 example 2 where binding of IgG recognition moiety is taught to diagnostic elements= electrodes).

Regarding claims 35 and 38 Mroczkowski et al. do not teach wherein the circuit further comprises a diode or non-linear component permitting current flow through the electronic module only in the direction from the first group of conductors to the second group of conductors.

Regarding claim 38, Mroczkowski et al. also do not teach

2) whereby a current flowing between one conductor of the first group to the one conductor of the second group of conductors defines a single junction point between them;

Regarding claims 35 and 38 Olsen teaches wherein the circuit further comprises a diode or non-linear component permitting current flow through the electronic module only in the direction from the first group of conductors to the second group of conductors (see abstract).

Regarding claim 38, by teaching diode Olsen inherently teaches whereby a current flowing between one conductor of the first group to the one conductor of the second group of conductors defines a single junction point between them (this is because most modern diodes are based on semiconductor p-n juntions. In a p-n diode, conventional current can flow from the p-type side (the anode) to the n-type side (cathode), but cannot flow in the opposite direction, thus a current flowing between one conductor of the first group to the one conductor of the second group of conductors defines a single junction point between them);

Regarding claim 41, Mroczkowski et al. teach wherein different assay sets of electrodes or different groups of assay sets are for assaying different targets (see page 5 lines 6-9 where different targets are taught). (see fig. 8 and 9 where multiplexing is taught and measurement of conductance from each assay set is performed using ohmmeter).

It would have been prima facie obvious to one of ordinary skill in the art to incorporate the in circuit ohmmeters containing diode taught by Olsen into the system taught by Mroczkowski et al. at the time the invention was made. The motivation to do so is provided to one of ordinary skill in the art by both Olsen as well as the art itself.

Art teaches one of ordinary skill that diode is a two-terminal device that have two active electrodes between which the signal of interest may flow, and most are used for their unidirectional electric current property. According to Wikipedia the most common function of a diode is to allow an electric current to pass in one direction and to block it in the opposite direction (reference

downloaded on August 13, 2008 provided). Thus, the diode can be thought of as an electronic version of a check valve. In view of this knowledge and teaching by Olsen that a circuit that has a plurality of diodes connected across the input terminals serve as a current generator protection circuit (see abstract), one of ordinary skill in the art can immediately see the advantage of using the diodes in the system taught by Mroczkowski et al. By using the diodes the integrated circuits present in the microelectronic device would be electrically isolated from each other so measurement of electrical conductance at each junction would be independent and unaffected by the measurement at any other junction.

14. Claims 36, 53-54 and 60-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mroczkowski et al. (WO 90/05300; cited in the IDS) and Olsen (US pat. 5,614,832 issued March 25, 1997 -previously cited) as applied to claims 35 and 37 above further in view of Hollis et al. (U.S. Patent No. 5,653,939 A- previously cited).

Regarding claim 36, Mroczkowski et al. and Olsen teach the device of claim 35, but do not teach wherein distance of center of one assay set to a center of an adjacent assay set is 100 μm or less.

Regarding claim 36, Hollis et al. teach wherein distance of center of one assay set to a center of an adjacent assay set is 100 μm or less (see col. 6 line 15-18 where a spacing of 2 microns is taught between the array of 2 micron wide wells. Thus teaching wherein distance of center of one assay set to a center of an adjacent assay set is 100 μm or less).

Regarding claim 53, Mroczkowski et al. and Olsen teach the device of claim 35, but do not teach wherein said recognition moiety is a nucleic acid molecule.

Regarding claims 53, 54 Hollis et al. teach wherein said recognition moiety is a nucleic acid molecule (see col. 6 lines 42-52).

Regarding claims 60, 62 Hollis et al. teach wherein said means comprises a computer (see col. 7 line 4 where computer is taught).

Regarding claim 61, 63 Hollis et al. teach wherein said means comprises a scanner for analyzing a plurality of assay sets (see col. 12 lines 10-12 where scanner is taught).

It would have been prime facie obvious to one of ordinary skill in the art to combine the computer taught by Hollis et al. in the microelectronic system taught by Mroczkowski et al. and Olsen at the time the invention was made. The motivation to do so is provided by Hollis et al. who state “The present invention can be used in connection with detection of targets which are molecular structures other than DNA or RNA, such as cells and antibodies.-----The technology described here employs those well understood binding interactions in a new microelectronic detection scheme. The commercial application of the methodology is for use to detect the presence of any of hundreds of thousands of different antibodies or other proteins, simultaneously, in a blood sample or other biological fluid. This is particularly useful in blood typing, the detection of viral infection such as AIDS, or the diagnosis of cancer." (see col. 18 lines 3-53). Thus one of ordinary skill can immediately see the advantages of using a computer to

process the huge amount of data that will be generated using these micro fabricated device resulting in more accurate, cheaper, faster and more efficient processing of multiple clinical samples as compared to manually recording the conductivity measurements obtained from the microelectronic circuits taught by Mroczkowski et al. and Olsen.

15. Claim 39 is rejected under 35 U.S.C. 103(a) as being unpatentable over over Mroczkowski et al. and Hollis et al. as applied to claim 24 further in view of Olsen (US pat. 5,614,832 issued March 25, 1997- previously cited).

Regarding claim 39, Mroczkowski et al. and Hollis et al. teach method of claim 24, wherein said device is an electronic device for determining one or more targets in a sample.

Regarding claim 39, Mroczkowski et al. teaches: an integrated circuit (see Fig. 8) comprising a first group of N1 conductors (see fig. 7 element 51 is first group of N1 conductors)

and a second group of N2 conductors (see fig. 7 element 52 is second group of N2 conductors), defining between them NlxN2 junctions (fig,. 7 element 53), each such junction being formed with an electronic module comprising two electrodes (fig. 8 layer 23 and 24 are electrodes), each electrode linked to or defined as an integral portion of one of the conductors (element 61 and 62 in Fig. 8 are conductors) and supported by a common substrate (base 22 in Fig. 8 is common substrate),

whereby a current flowing between one conductor of the first group to one conductor of the second group of conductors defines a single junction point

between them (see page 18 lines 9-21 where Fig. 9 is described); each pair of electrodes forming part of an array set (see fig. 8 where 23/24 each pair is shown to form an array set),

each array set having a recognition moiety for binding to a component of a target (see Fig 1 where between pair of electrodes 23A and 24A biogenic substance 30A such as antigenic 12A coated onto a non conductive base 22A is shown. Thus teaching each array set having a recognition moiety for binding to a component of a target);

Regarding claim 39 Mroczkowski et al. do not teach wherein the circuit further comprises a diode or non-linear component permitting current flow through the electronic module only in the direction from the first group of conductors to the second group of conductors.

Regarding claim 39, Mroczkowski et al. also do not explicitly recite

whereby a current flowing between one conductor of the first group to the one conductor of the second group of conductors defines a single junction point between them;

Regarding claim 39 Olsen teaches wherein the circuit further comprises a diode or non-linear component permitting current flow through the electronic module only in the direction from the first group of conductors to the second group of conductors (see abstract).

Regarding claim 39, by teaching diode Olsen inherently teaches whereby a current flowing between one conductor of the first group to the one conductor of the second group of conductors defines a single junction point between them

(this is because most modern diodes are based on semiconductor p-n juntions. In a p-n diode, conventional current can flow from the p-type side (the anode) to the n-type side (cathode), but cannot flow in the opposite direction, thus a current flowing between one conductor of the first group to the one conductor of the second group of conductors defines a single junction point between them);

It would have been prima facie obvious to one of ordinary skill in the art to incorporate the in circuit ohmmeters containing diode taught by Olsen into the system taught by Mroczkowski et al. and Hollis et al. at the time the invention was made. The motivation to do so is provided to one of ordinary skill in the art by both Olsen as well as the art itself.

Art teaches one of ordinary skill that diode is a two-terminal device that have two active electrodes between which the signal of interest may flow, and most are used for their unidirectional electric current property. According to Wikipedia the most common function of a diode is to allow an electric current to pass in one direction and to block it in the opposite direction (reference downloaded on August 13, 2008 provided). Thus, the diode can be thought of as an electronic version of a check valve. In view of this knowledge and teaching by Olsen that a circuit that has a plurality of diodes connected across the input terminals serve as a current generator protection circuit (see abstract), one of ordinary skill in the art can immediately see the advantage of using the diodes in the system taught by Mroczkowski et al. and Hollis et al. By using the diodes the integrated circuits present in the microelectronic device would be electrically isolated from each other so measurement of electrical conductance at each

junction would be independent and unaffected by the measurement at any other junction.

Conclusion

16. All claims 1, 4-9, 18-20, 22-28, 35-39, 41, 43-45, 47-51, 53-57, 60-63 and 65 under consideration are rejected over prior art.

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUCHIRA PANDE whose telephone number is (571)272-9052. The examiner can normally be reached on 8:30 am -5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax

phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Suchira Pande
Examiner
Art Unit 1637

/Teresa E Strzelecka/

Primary Examiner, Art Unit 1637

April 27, 2009